## CLAIMS

1. A PI3Kγ crystal with unit dimensions of a=143.3 Å, b=67.6 Å, c=107.0 Å, and β=95.9°.

2. A method of modulating phospholipid substrate binding to PI3Kγ, comprising:

modifying the phospholipid domain of PI3Kγ, said domain comprising the C-terminal helix kα12, catalytic loop, and activation loop.

3. A method of claim 2, wherein modifying comprises contacting an antibody specific-for said phospholipid binding domain.

4. An isolated polypeptide fragment of a PI3Kγ consisting essentially of a phospholipid binding domain, comprising the C-terminal helix kα12, catalytic loop, and activation loop.

5. An isolated polypeptide fragment of claim 4, comprising: amino acids 943-951 of the catalytic loop and amino acids 964-988 of the activation loop.

6. An isolated polypeptide mutein comprising a phospholipid binding domain, which domain comprises the C-terminal helix kα12, catalytic loop, and activation loop of Fig. 3, and at least 95% sequence identity to the remaining sequence in Fig. 3.

7. An isolated polypeptide fragment of claim 6, wherein said the amino acids at position Lys807, Lys808, Arg947, or Lys973 are mutated, and such fragment has less than normal phospholipid binding activity.

8. An antibody which is specific for the phospholipid binding domain of claims 4-7.

9. A nucleic acid coding for a polypeptide of claims 4-7.

10. A method of modulating lipid kinase catalysis, comprising: modifying His968 of a PI3Kγ.

11. A method of claim 10, wherein modifying comprises contacting an antibody specific-for an amino acid region comprising His968.

12. A method of claim 10, wherein said modifying comprises substituting His968 with a non-conservative amino acid.

13. An isolated polypeptide of a PI3Kγ, consisting essentially of 8-100 amino acids, comprising His968.

14. A PI3Kγ polypeptide mutein, comprising a sequence having at least 95% amino acid sequence identity to Fig. 3, and having a His968.

15. An antibody which is specific for the isolated polypeptide of claims 13-14.

16. A nucleic acid coding for a polypeptide of claim 13-14.

17. A method of modulating RAS activity in activating the PI3Kγ, comprising:

modifying the kβ1-kβ2, kβ4-kβ5, kα6, Rα2 and Rβ3 -Rβ4 domains of said PI3Kγ.

18. A method of claim 17, comprising modifying Lys234, Asp238, and Lys255

19. A method of claim 17, comprising contacting an antibody specific-for a peptide comprising amino acids Lys234, Asp238, and Lys255.

20. An isolated polypeptide fragment of PI3Kγ consisting essentially of the kβ1-kβ2, kβ4-kβ5, kα6, Rα2 and Rβ3 -Rβ4 domains of said PI3Kγ.

21. A polypeptide mutein of a PI3Kγ comprising the kβ1-kβ2, kβ4-kβ5, kα6, Rα2 and Rβ3 -Rβ4 domains, Lys234, Asp238, and Lys255, of Fig. 3, and at least 95% sequence identity to the remaining sequence in Fig. 3.

22. An antibody which is specific-for said polypeptide of claims 20-21.

23. A nucleic acid coding for a polypeptide of claims 20-21.

24. A method of inhibiting the binding of PI3Kγ to cell membranes, comprising:

modifying an amino acid a) the lining the crevice region between the N- and C-lobes; b) the CBR regions; or c) the region comprising tip of the activation loop.

25. A method of claim 24, wherein the modifying comprises contacting said amino acid with an antibody specific-for said regions.

26. An isolated polypeptide fragment of a PI3Kγ consisting essentially of a) the lining the crevice region between the N- and C-lobes; b) the CBR regions; or c) the region comprising tip of the activation loop.

27. A polypeptide mutein of a PI3Kγ comprising the lining the crevice region between the N- and C-lobes; b) the CBR regions; or c) the region comprising tip of the activation loop of Fig. 3, and at least 95% sequence identity to the remaining sequence in Fig. 3.

28. An antibody which is specific-for said polypeptide of claims 26-27.

29. A nucleic acid coding for a polypeptide of claims 26-27.

30. A method of modulating protein-protein interactions with PI3Kγ, comprising

modifying the surfaces of the B-helices.

31. A method of claim 30, wherein the B-helices are hB1, hB1', hB2, hB2', hB3, hB4, or hB5.

32. A method of claim 30, wherein the modifying comprises contacting said amino acid with an antibody specific-for hB1, hB1', hB2, hB2', hB3, hB4, or hB5.

33. An isolated polypeptide fragment of a PI3Kγ consisting essentially of hB1-hB5.

34. A polypeptide mutein of a PI3Kγ comprising hB1-hB5 of Fig. 3, and at least 95% sequence identity to the remaining sequence in Fig. 3.

35. An antibody which is specific-for a polypeptide of claims 33-34.

36. A nucleic acid coding for a polypeptide of claims 33-34.